



Pipeline and Hazardous Material Administration (PHMSA)

Department of Transportation AN ICCVAM UPDATE

Presented at the Public Forum, NIH Natcher Center, MD

May 23, 2017

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Regulatory Classification: PHMSA DOT 49 CFR § 173.

	<u>Route</u>	<u>Hazard Zone</u>	<u>Packing Group</u>
Acute Toxicity	Inhalation (LC ₅₀)	A	I
		B	I
		C	II
		D	III
	Ingestion (LD ₅₀) Dermal (LD ₅₀)		I, II, III
Corrosivity	Skin		I, II, III



CLASSIFICATION

Inhalation

Gas	Division 2.3	Hazard Zone A	Hazard Zone B	Hazard Zone C	Hazard Zone D
		Arsine	Chlorine	Sulfur Dioxide	Ammonia
		LC50≤200ppm	200ppm<LC50≤1000ppm	1000 ppm≤LC50≤3000ppm	3000ppm<LC50≤5000ppm

Dust & Mists	Division 6.1	Packing Group I	PG II	PG III
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Gas vaporized From Liquids	Division 6.1	Hazard Zone A	Hazard Zone B	Hazard Zone C	Hazard Zone D
		The hazard zone determined from toxicity and volatility .			





CLASSIFICATION for Division 6.1 (Continued)

<u>Packing Group</u>	<u>Oral Ingestion (LD₅₀, mg/kg)</u>	<u>Dermal Absorption (LD₅₀, mg/kg)</u>
I	LD ₅₀ ≤ 5.0	LD ₅₀ ≤ 50
II	5 < LD ₅₀ ≤ 50	50 < LD ₅₀ ≤ 200
III	50 < LD ₅₀ ≤ 300	200 < LD ₅₀ ≤ 1000



Animal Ranking (in order of preference)

(Taken from an open, non-DOT publication)

Rat

Mouse

Rabbit

Guinea Pig

Cat

Dog

Monkey



EXAMPLE: ACUTE TOXICITY DATA for Ammonia Gas (Source: CDC) Lethal concentration data:

Species	Reference	LC50(ppm)	LCLo(ppm)	Time	Adjusted 0.5-hr LC (CF)	Derived Value
Rat	Alarie 1981	40,300	-----	10 min	23,374 ppm (0.58)	2,337 ppm
Rat	Alarie 1981	28,595	-----	20 min	23,448 ppm (0.82)	2,335 ppm
Rat	Alarie 1981	20,300	-----	40 min	23,345 ppm (1.15)	2,335 ppm
Rat	Alarie 1981	11,590	-----	1 hr	16,342 ppm (1.41)	1,634 ppm
Rat	Back et al. 1972	7,338	-----	1 hr	10,347 ppm (1.41)	1,035 ppm
Mouse	Back et al. 1972	4,837	-----	1 hr	6,820 ppm (1.41)	682 ppm
Rabbit	Boyd et al. 1944	9,859	-----	1 hr	13,901 ppm (1.41)	1,309 ppm
Cat	Boyd et al. 1944	9,859	-----	1 hr	13,901 ppm (1.41)	1,309 ppm
Rat	Deichmann and Gerarde 1969	2,000	-----	4 hr	5,660 ppm (2.83)	566 ppm
Mammal	Flury 1928	-----	5,000	5 min	2,050 ppm (0.41)	205 ppm
Mouse	Kapeghian et al. 1982	4,230	-----	1 hr	5,964 ppm (1.41)	596 ppm
Human	Tab Biol Per 1933	-----	5,000	5 min	2,050 ppm (0.41)	205 ppm



Variation of Ammonia Acute Toxicity Data

LC₅₀ (ppm) 1 hour exposure

Rat 4000*, 7,338**, 11,590

Mouse 4230, 4837

Cat 9,859

* Conversion Factor of n=2 (based on ten Berge et al. 1986)

** CGA listed value

Human Fatality Data: Fatalities reported from spills from tanks,
storage, rail, etc: 6 locations.

Classification of Anhydrous Ammonia: Domestically 2.2; Internationally TIH



SKIN CORROSIVITY

Classification - Class 8, and further subdivided into PG I PG II PG III.

Corrosive Substances – substances which, by chemical action, will cause severe damage when in contact with living tissue, or, in the case of leakage, will materially damage, or even destroy, other goods or the means of transport.

PG I - Materials that cause full thickness destruction of intact skin tissue within an observation period of up to 60 minutes starting after the exposure time of three minutes or less.

PG II – Materials other than those meeting PG I criteria that cause full thickness destruction of intact skin tissue within an observation period of up to 14 days starting after the exposure time of more than three minutes but not more than 60 minutes.

PG III - Materials other than those meeting PG I or II criteria that cause full thickness destruction of intact skin tissue within an observation period of up to 14 days starting after the exposure time of more than 60 minutes but not more than 4 hr.



TEST GUIDELINES FOR ACUTE TOXICITY

- Inhalation

Test Method not specifically specified

OECD TG 403 (Dusts and Aerosol) – Acute Inhalation Toxicity Acceptable
OECD TG 436 (Acute Toxic Gas Method)

- Oral

OECD TG 423 – Acute Oral Toxicity – Acute Toxic Class Method
OECD TG 420 - Fixed Dose Procedure
OECD TG 425 – Acute Oral Toxicity : Up-and-Down Procedure

No In-Vitro Method at this point.



TEST GUIDELINES FOR CORROSIVITY

DOT E-10904 – An In Vitro alternative to the In Vivo method.

OECD TG 404 – In Vivo method

OECD TG 435 – “In Vitro Membrane Barrier Test Method for Skin Corrosion” 2006

OECD TG 430 – “In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)” 2004.

OECD TG 431 – “In Vitro Skin Corrosion: Human Skin Model Test” 2004.



Comparison of Packing Group Defined by In Vivo Studies and the Corrosive Test.

In Vivo Packing Group

	I	II	III	NC	Total
I	3	1	1	0	5
II	1	28	1	7	37
III	0	0	1	8	9
Non-corrosive	1	0	0	38	39
Total	5	29	3	53	90

**Corrositex
 Packing Group**



OBSERVATIONS

- **Challenge: How to interpret animal data to human effects for acute toxicity**
- **Skin corrosivity for determining PGs – More innovative approaches needed.**

